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PAUL J WHITE, SENIOR COUNSEL
NATIONAL RENEWABLE ENERGY LABORATORY (NREL)
1617 COLE BOULEVARD
GOLDEN, CO 80401-3393

EXAMINER

RAO, MANJUNATH N

ART UNIT PAPER NUMBER

1652

DATE MAILED: 11/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--|-------------------------------------|--|
| Office Action Summary | Application No. 09/917,384 | Applicant(s) ADNEY ET AL. | |
| | Examiner Manjunath N. Rao, Ph.D. | Art Unit 1652 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11, 14-21, 23-25, 28-35, 44, 45 and 69-84 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11, 14-21, 23-25, 28-35, 44, 45 and 69-84 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Sequence alignments</u> . |

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9-6-05 has been entered.

Claims 1-11, 14-21 23-25, 28-35, 44-45, 69-78, new claims 79-84 are still at issue and are present for examination.

Applicants' amendments and arguments filed on 9-6-05, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Sequence Compliance

It is noted that applicant has filed a sequence listing on 9-6-05. However, it is not clear to the Examiner as to why the sequence listing was filed now and whether said sequence listing is identical to that filed previously on 11-27-02 or whether said sequence listing is an amended version. Examiner requests a clarification as to why this sequence listing has been filed and a statement from the applicant that the newly filed sequence listing is identical in all respects to the sequence listing filed earlier on 11-27-02.

Claim Objections

Claim 78 is objected to because of the following informalities: Claim 78 is drawn to a composition comprising in combination “a sequence of SEQ ID NO:4, 5, and 7”. However, claim 11 improperly recites SEQ ID NO:2 as an amino acid sequence. It can be seen from the sequence listing that SEQ ID NO:2 is a polynucleotide and not a polypeptide. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1, 6 and claims 2-5, 7-11, 14-21, 23-25, 44-45, 69-78, which depends from claim 1 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 6 recite the phrase “comprising a glycoside hydrolase 48 family catalytic domain”. The metes and bounds of the phrase is not clear to the Examiner. The catalytic domain of GH48 family of proteins may comprising more than one specific type of activity even though all such activities can be classified as a “glycoside hydrolase activity”. Therefore, the specific activity encompassed by the above phrase is not clear to the Examiner. Examiner urges applicants to provide a specific activity for the claimed polypeptide.

Claims 75, 78 and claim 76 which depends on claim 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and

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distinctly claim the subject matter which applicant regards as the invention. Claims 75, 78 is drawn to a composition comprising in combination “a sequence ofSEQ ID NO:4/ 5, and 7” (see line 3 and line 2 respectively in claims 75 and 78). The sub-phrase “a sequence of” in the phrase above leads to some confusion in that it is not clear to the Examiner whether the composition comprises “a sequence of amino acid sequence SEQ ID NO:4/5, meaning a fragment of SEQ ID NO:4/5 or the full length of SEQ ID NO:4/5. Examiner suggests amending the above phrase to “the sequence” which makes it clear that the entire length of SEQ ID NO:4 is comprised in the composition.

Claims 76-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 76-77 recite the phrase “further defined as the sequence of..”. The metes and bounds of the phrase is not clear to the examiner. It is not clear to the Examiner whether applicants are making a direct reference to the respective SEQ ID NO in the claims or whether the SEQ ID NO of the sequences claimed are representative of a genus of the sequence in the claim. Examiner suggests applicants to delete the phrase and refer to the SEQ ID NO directly.

Claim 81 and claims 82 and 84 which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 81 recites the limitation "peptide" in line 1. There is insufficient antecedent basis for this limitation in the claim. Examiner suggests amending “peptide” to “polypeptide”.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-20, 79-84 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 17-20, 79-84 are drawn to an polypeptide sequences that are 95%, 98% identical to SEQ ID NO:1, 2, 4, 5, 6, 7. However, a perusal of the specification indicates that applicants have no support for the newly added “95% or 98% identity” language which now constitutes a “new matter”. Therefore claims 17-20, 79-84 are rejected for introducing “new matter” into the claims. Either under “remarks” section or in the claims, applicants provide no guidance for the examiner to identify support for the above amendments in the specification. A perusal of the specification indicated support for only “90% identity” language and that too for only SEQ ID NO:1 (page 18 of the specification). However, Examiner was unable to find the support for “98% identity” language for either SEQ ID NO:1 or for the other sequences.

Claims 1-5, 14-16, 20-21, 28-35, 44-45, 70-74, 79-84 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a Gux 1 polypeptide comprising the specific catalytic domain of an exoglucanase, i.e., full length SEQ ID NO:5 or a polypeptide comprising an amino acid sequence 98% identical to SEQ ID NO:5, further comprising a CBD-III domain with SEQ ID NO:4 or an amino acid sequence that is 98%

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identical to SEQ ID NO:4 and a CBD-II domain with SEQ ID NO:7 or an amino acid sequence that is 98% identical to SEQ ID NO:7, or a peptide having SEQ ID NO:1 or an amino acid sequence that is 98% identical to SEQ ID NO having the specific catalytic activity of an exoglucanase encoded by a nucleic acid sequence with SEQ ID NO:2, does not reasonably provide enablement for any or all such Gux I peptide comprising 1) any catalytic domain of the GH48 family hydrolase with any 637 to about 643 amino acids in length or 2)any CBDIII domain that is about 150-156 amino acids in length or 3) any CBDII domain that is 95-105 amino acids in length or 4) an amino acid sequence (without any function attached to said polypeptide) encoded by a polynucleotide that is 90% identical to SEQ ID NO:2, or 5) a Gux1 peptide comprising any GH48 family catalytic domain and an amino acid sequence that is 70%, 80%, 90% to SEQ ID NO:5 or 6)a peptide comprising amino acid sequence that is 90% or at least 98% identical to SEQ ID NO:4, 5, 6, 7 or 1 (without any attached function of such polypeptides), or 7)fusion polypeptides of the above polypeptides comprising a heterologous polypeptide such a peptide tag, or a substrate targeting moiety or leucine zipper or a composition comprising such polypeptides along with a carrier (without any attached function of such polypeptides). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

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prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-5, 14-16, 20-21, 28-35, 44-45, 70-74, 79-84 are so broad as to encompass any polypeptide with or without any specific function or a polypeptide comprising any catalytic domain (i.e., any type of activity within the GH48 family) of any 637 to about 643 amino acids in length or any CBDIII domain that is about 150-156 amino acids in length or any CBDII domain that is 95-105 amino acids in length or an amino acid sequence encoded by a polynucleotide that is 90% identical to SEQ ID NO:2, or a Gux1 peptide comprising any GH48 family catalytic domain and an amino acid sequence that is 70%, 80%, 90% to SEQ ID NO:5 or a peptide comprising amino acid sequence that is 90% or at least 98% identical to SEQ ID NO:4, 5, 6, 7 or 1 (without any attached function of such polypeptides), or fusion polypeptides of the above polypeptides comprising a heterologous polypeptide such a peptide tag, or a substrate targeting moiety or leucine zipper or a composition comprising such polypeptides along with a carrier (without any attached function of such polypeptides).

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of Gux1 polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is

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limited to the nucleotide and encoded amino acid sequence of only one such Gux1 having an amino acid sequence, SEQ ID NO:1, encoded by polynucleotide SEQ ID NO:2, wherein the polypeptide has a specific activity, beta 1-4 exoglucanase activity. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides some even with an undefined function/activity. The specification is limited to teaching use of SEQ ID NO: 1 or a polypeptide comprising polypeptides with SEQ ID NO:4, 5 and 7 as a Gux1 polypeptide with exoglucanase activity but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

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The specification does not support the broad scope of the claims which encompass all modifications and fragments of any glycosylhydrolase polypeptide as described in the above paragraphs because the specification does not establish: (A) regions of the protein structure which may be modified without effecting either the exoglucanase catalytic activity or the cellulose binding activity of the CBD domains; (B) the general tolerance of exoglucanase such as cellulase or endoglucanases and the CBDs to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any exoglucanase or any CBD polypeptide amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including exoglucanase catalytic domains, and cellulose binding domains with an enormous number of amino acid modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have traversed the above rejection basically arguing that claims are enabled. Applicants maintain the same line of argument as in previous responses that the specification provides guidance. They point to Table 3, page 17, 19

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etc. and argue that the Office is simply wrong in assuming that the specification fails to disclose a representative species. Applicants have also filed new claims and argue that those claims also have sufficient enablement support.

Examiner respectfully disagrees with the above line of argument. While it can be agreed that applicant provides table 3 with a comparison of sequences and general guidance regarding the beginning and ending of different domains on the polypeptide as on page 19 of the specification, such guidance is not enough for those skilled in the art to make enormous changes in the amino acids as claimed in the instant claims. Guidance as to which specific amino acid in the sequence can be modified by substituting which other specific amino acid or which specific amino acid can be modified by deletion or insertion of other specific amino acid is entirely missing from the specification. Examiner has already indicated in his rejection that methods to make variants by site directed mutagenesis etc. are well known in the art, however, without specific guidance as to which specific amino acid can be modified, one of ordinary skill in the art will suffer from undue experimentation to arrive at the variants of polynucleotides and polypeptides claimed herein. In order to produce variants as claimed by applicants it requires that one of ordinary skill in the art know or be provided with specific guidance regarding the amino acid residues in the sequence that can be modified without affecting its activity (in the instant case the exoglucanase) and guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities of the amino acid sequences. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required,

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the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting either the catalytic activity or the cellulose binding activity of the CBD domains; (B) the general tolerance of exoglucanase, and the CBDs to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any exoglucanase or any CBD polypeptide amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Hence the above rejection is maintained.

Claims 1-9, 14-21, 23-25, 69-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-9, 14-21, 23-25, 69-74 are directed to composition comprising a Gux1 peptide wherein said Gux1 peptide comprises a catalytic domain GH48 family glycoside hydrolase of 637 to 643 amino acids in length, a carbohydrate binding domain CBD type III of 15-156 amino acids in length and a CBD type II of 95-105 amino acids in length and fusion polypeptides of the same fused to heterologous polypeptides all of which encompass variants, mutants and recombinants. Claims 1-9, 14-21, 23-25, 69-74 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides including modified polypeptide

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sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue (i.e., variants and mutants) that have not been disclosed in the specification. No description has been provided of even a representative number of polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:1 or characterization of SEQID NO:4-7 as catalytic domains and CBD domains, has been provided by applicants which would indicate that they had possession of the claimed genus of all the polypeptides. The specification does not contain any disclosure of the specific structure of the polypeptide sequences, including fragments and variants within the scope of the claimed genus or identifying information that the structure of SEQ ID NO:1 is representative of all the species claimed herein. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicants have traversed the above rejection arguing that patents need not teach what is already well known in the art, that those skilled in the art would have the knowledge to modify the amino acid sequence with SEQ ID NO:1 and that

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such techniques for modification are well known. Applicants also argue that they are not required to disclose each and every species encompassed by the claims and that it does suffice that the applicant has presented a structural rationale. Applicants also argue that they fail to understand how the Office distinguishes the Enzo/Amgen case premise of law on the facts of this case. Applicants argue that Dr. Himmel's declaration provides evidence that something like 132,000 combinations of structure are obtainable within the level of ordinary skill and guidance provided in the specification. Applicants argue that the Office has merely repeated the prior rejection without addressing the above points and urges the Office to point particularly the specific guideline in question in the written description guidelines at www.uspto.gov.

Examiner has in fact rewritten the above rejection so that it makes it clear to the applicants as to why the above rejection has been applied. While it is agreed that applicants need not disclose each and every species encompassed by the claims Examiner respectfully disagrees with the argument that it does suffice that the applicant has presented a structural rationale. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical **and/or** chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to

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reflect the variation within the genus. Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genera includes species which are widely variant in structure (including all those that disclosed in the different the electronic databases recited in the Declaration by Himmel) as well as function (i.e., exoglucanase, endoglucanase, beta-glucosidase etc. which are all highly specific activities). The genus of the polypeptides and polynucleotides in above claims is structurally diverse as it encompasses polypeptides with Gux1, cellulose binding activity from all or any source including variants that are of the different amino acid lengths and variant in function by encompassing the function of all catalytic activities encompassed in GH48 family. As such, neither the description of the function alone of the Gux1 polypeptide or the structure alone nor the disclosure solely of generalized functional features (glycoside hydrolase) present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus.

The Declaration filed by Dr. Himmel is also not persuasive to overcome the above rejection. This is because while the Declaration declares that the three domains are well known and that those practicing the art can arrive at the sequences by going to the CAZy database web site it does not address providing the description of the structure of variants and mutants encompassed in the above claims along with the associated specific function/activity of the polypeptide. In the instant case, for example, claims are haphazardly drawn to polypeptides

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having structural identification but lacking function or functional identification but lacking structural information. In order to satisfy written description requirement, claims need to recite and reiterate structure and function. In order to aid the applicant understand the written description issues Examiner directs them specifically to examples 13 and 14 in the Written Description guidelines at www.uspto.gov. However, for the time being the above rejection is maintained.

Claims 28-35, 44-45, 70-74, 79-84 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 28-35, 44-45, 70-74, 79-84 are directed to composition comprising an amino acid with SEQ ID NO:4, 5, 6, or 7 or polypeptides comprising amino acid sequences that are 90%, 95%, 98% identical to SEQ ID NO: 1, 2, 4, 5, 6, or 7 and fusion polypeptides comprising the above amino acid sequences.

Claims 28-35, 44-45, 70-74, 79-84 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides whose function has not been described. No description has been provided of the all the polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:1 and 5 as a Gux1 polypeptide with a glycosylhydrolase activity or partial characterization of SEQID NO:4 and 7 as having cellulose binding activity, has been provided by applicants which would indicate that they had possession of the claimed genus of all the polypeptides. The specification does not

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contain any disclosure of the function of all the polypeptide sequences, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of function. Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicants have traversed the above rejection arguing that applicants fail to understand the relevancy of the Office position because a wide range of utilities are also disclosed and it is permissible for a species or genus of composition to have a wide range of functionality. Applicants also take the position that a selection of useful modified peptides may be made based upon the claimed sequences, (for example, as recited in the paragraph beginning at line 23 on page 20), and that even if the modification of a peptide sequence results in rendering the peptide nonfunctional for its natural purpose, such peptides also have utility, for example, in fully characterizing the domain or in selectively blocking activity of the peptide in a competitive assay, which may be performed according to the last paragraph on page 17 of the Specification. Examiner fails to understand the logic behind such an argument because these are not claimed in the claims.

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Utilities or activities of modified peptides cannot be imagined by the Examiner and applicants also can claim polypeptides commensurate in scope with the support in the specification. In other words it appears that applicants argue that they are eligible for a patent to any polypeptide variant derived from the sequences recited in the claims even if said polypeptide loses its original function because any or all peptides indeed has some utility and therefore must be allowed even when such utility is outside of the scope of the claim.

Applicants also argue that Examiner incorrectly adopts as a *per se* rule what is only one way of making the requisite showing and that another way to do this is to adopt a structural rationale, for example, as disclosed in Table 3. Applicant argues that this is understood from the perspective of skill as encompassing a genus of variations, and Dr. Himmel's declaration is provided to show this is true. It is not clear to the Examiner as to what applicants are arguing here. However, in summary Examiner would like to reiterate that the written description requirement is satisfied when the claim recites both the structure **and** function of the claimed polynucleotide or polypeptide. Recitation solely of either the function alone or structure alone fails to satisfy the written description. In the instant case, claims haphazardly recite either the structure alone or the function alone or when a function is recited it is a broad function such as glycoside hydrolase, which fails to satisfy the written description requirement. Examiner suggests applicants refer to specific examples 13 and 14 in the Guidelines and encourages to call the Examiner by telephone if more assistance is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

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improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 28-35, 44-45 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20, 27, 43, 48-54, 63, 65-67 of U.S. Patent Application No.09/917383 (which has now been allowed) and claims 26, 27-34, 43-44, 63 of US Patent application No. 09/917378. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim, because the examined claim is either anticipated by, or would have been obvious over the reference claim. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 28-35, 44-45 of the instant application and claims 20, 27, 43, 48-54, 63, 65-67 of U.S. Patent Application No.09/917383 (which has now been allowed) and claims 26, 27-34, 43-44, 63 of US Patent application No. 09/917378 are all directed to polypeptide comprising SEQ ID NO:4 or an amino acid sequence having 90% sequence identity with SEQ ID NO:4. (Please note that SEQ ID NO:4 and 7 in the instant application have been found to be more than 90% identical to SEQ ID NO:1, 4 and 5 of Application 09/917,378 see enclosed sequence alignment, and 90% or more than 90%

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identical to SEQ ID NO:1 of US application No. 09/917,383 (see enclosed sequence alignment).

Among all the different polypeptide variants claimed in the instant application and in the reference patent a good number of variants are identical to one another. The portion of the specification (and the claims) in the reference applications that supports the recited amino acid sequences includes several embodiments that would anticipate the polypeptides claimed in claims 28-35, 44-45 herein. Claims of the instant application listed above cannot be considered patentably distinct over claims 20, 27, 43, 48-54, 63, 65-67 of U.S. Patent Application No.09/917383 (which has now been allowed) and claims 26, 27-34, 43-44, 63 of US Patent application No. 09/917378 when there is specifically recited embodiment that would anticipate mainly claims 28-35, 44-45 of the instant application. Alternatively, claims 28-35, 44-45 cannot be considered patentably distinct over claims of the reference applications when there is specifically disclosed embodiment in the reference applications that supports claims of those applications and falls within the scope of claims 28-35, 44-45 herein because it would have been obvious to one having ordinary skill in the art to modify claims of the reference applications by selecting a specifically disclosed embodiment that supports those claims. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within claims of the reference applications.

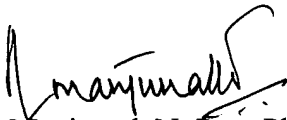
Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the

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examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

A handwritten signature in black ink, appearing to read 'Manjunath N. Rao', with a stylized flourish at the end.

Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

November 10, 2005

TYPE: PRT
US-09-917-384A-4
ORGANISM: Acidothermus cellulolyticus
Query Match
Best Local Similarity 100.0%; Score 819; DB 24; Length 153;
Matches 153; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 AVTLKAOYKNDSDAPSDNQIKPGLQVNTGSSVDLSTVTVRYWFTRDGSSSTLVYNCW 60
DB 1 AVTLKAOYKNDSDAPSDNQIKPGLQVNTGSSVDLSTVTVRYWFTRDGSSSTLVYNCW 60
QY 61 AAMGCGNIRASFGSVNPATPTADTYLQLSFTGTTAAGSGTGEIQNRVKNKSDWSNFDN 120
DB 61 AAMGCGNIRASFGSVNPATPTADTYLQLSFTGTTAAGSGTGEIQNRVKNKSDWSNFDN 120
QY 121 DYSYGTNTTFQDWTKVTVYVNGVLVWGTEPSGA 153
DB 121 DYSYGTNTTFQDWTKVTVYVNGVLVWGTEPSGA 153

RESULT 2
US-09-917-384A-1
Sequence 1, Application US/09917384A
GENERAL INFORMATION:
APPLICANT: ADNEY, WILLIAM S.
APPLICANT: DING, SHI-YOU
APPLICANT: MCCARTER, SUZANNE
APPLICANT: HIMMEL, MICHAEL E.
APPLICANT: DECKER, STEPHEN R.
APPLICANT: VINZANT, TODD B.
TITLE OF INVENTION: THERMAL TOLERANT EXOGLUCANASE FROM ACIDOTHERMUS
TITLE OF INVENTION: CELLULOLYTICUS
FILE REFERENCE: NREL 01-38
CURRENT APPLICATION NUMBER: US/09/917,384A
CURRENT FILING DATE: 2001-07-28
NUMBER OF SEQ ID NOS: 11
SOFTWARE: PatentIn Ver. 2.1
SEQ ID NO 1
LENGTH: 1121
TYPE: PRT
ORGANISM: Acidothermus cellulolyticus
US-09-917-384A-1
Query Match
Best Local Similarity 100.0%; Score 819; DB 24; Length 1121;
Matches 153; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 AVTLKAOYKNDSDAPSDNQIKPGLQVNTGSSVDLSTVTVRYWFTRDGSSSTLVYNCW 60
DB 35 AVTLKAOYKNDSDAPSDNQIKPGLQVNTGSSVDLSTVTVRYWFTRDGSSSTLVYNCW 94
QY 61 AAMGCGNIRASFGSVNPATPTADTYLQLSFTGTTAAGSGTGEIQNRVKNKSDWSNFDN 120
DB 95 AAMGCGNIRASFGSVNPATPTADTYLQLSFTGTTAAGSGTGEIQNRVKNKSDWSNFDN 154
QY 121 DYSYGTNTTFQDWTKVTVYVNGVLVWGTEPSGA 153
DB 155 DYSYGTNTTFQDWTKVTVYVNGVLVWGTEPSGA 187

RESULT 3
US-09-917-383-1
Sequence 1, Application US/09917383
GENERAL INFORMATION:
APPLICANT: DING, SHI-YOU
APPLICANT: ADNEY, WILLIAM S.
APPLICANT: VINZANT, TODD B.
APPLICANT: DECKER, STEPHEN R.
APPLICANT: HIMMEL, MICHAEL E.
TITLE OF INVENTION: THERMAL TOLERANT CELLULOSE FROM ACIDOTHERMUS
TITLE OF INVENTION: CELLULOLYTICUS
FILE REFERENCE: 40170.6US01

CURRENT APPLICATION NUMBER: US/09/917,383
CURRENT FILING DATE: 2001-07-28
NUMBER OF SEQ ID NOS: 14
SOFTWARE: PatentIn Ver. 2.1
SEQ ID NO 1
LENGTH: 1228
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Description of Artificial Sequence: Segment of
OTHER INFORMATION: GUXA
US-09-917-383-1
Query Match
Best Local Similarity 96.1%; Score 787; DB 24; Length 1228;
Matches 146; Conservative 0; Mismatches 3; Indels 0; Gaps 0;
QY 4 LKAOYKNDSDAPSDNQIKPGLQVNTGSSVDLSTVTVRYWFTRDGSSSTLVYNCW 63
DB 588 LKAOYKNDSDAPSDNQIKPGLQVNTGSSVDLSTVTVRYWFTRDGSSSTLVYNCW 647
QY 64 GCGNIRASFGSVNPATPTADTYLQLSFTGTTAAGSGTGEIQNRVKNKSDWSNFDN 123
DB 648 GCGNIRASFGSVNPATPTADTYLQLSFTGTTAAGSGTGEIQNRVKNKSDWSNFDN 707
QY 124 YGTNTTFQDWTKVTVYVNGVLVWGTEPSG 152
DB 708 YGTNTTFQDWTKVTVYVNGVLVWGTEPSG 736

RESULT 4
US-09-917-384-1
Sequence 1, Application US/09917384
GENERAL INFORMATION:
APPLICANT: DING, SHI-YOU
APPLICANT: ADNEY, WILLIAM S.
APPLICANT: VINZANT, TODD B.
APPLICANT: DECKER, STEPHEN R.
APPLICANT: HIMMEL, MICHAEL E.
TITLE OF INVENTION: THERMAL TOLERANT CELLULOSE FROM ACIDOTHERMUS
TITLE OF INVENTION: CELLULOLYTICUS
FILE REFERENCE: 40170.6US01
CURRENT APPLICATION NUMBER: US/09/917,384
CURRENT FILING DATE: 2001-07-28
NUMBER OF SEQ ID NOS: 14
SOFTWARE: PatentIn Ver. 2.1
SEQ ID NO 1
LENGTH: 1228
TYPE: PRT
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Description of Artificial Sequence: Segment of
OTHER INFORMATION: GUXA
US-09-917-384-1
Query Match
Best Local Similarity 96.1%; Score 787; DB 24; Length 1228;
Matches 146; Conservative 0; Mismatches 3; Indels 0; Gaps 0;
QY 4 LKAOYKNDSDAPSDNQIKPGLQVNTGSSVDLSTVTVRYWFTRDGSSSTLVYNCW 63
DB 588 LKAOYKNDSDAPSDNQIKPGLQVNTGSSVDLSTVTVRYWFTRDGSSSTLVYNCW 647
QY 64 GCGNIRASFGSVNPATPTADTYLQLSFTGTTAAGSGTGEIQNRVKNKSDWSNFDN 123
DB 648 GCGNIRASFGSVNPATPTADTYLQLSFTGTTAAGSGTGEIQNRVKNKSDWSNFDN 707
QY 124 YGTNTTFQDWTKVTVYVNGVLVWGTEPSG 152
DB 708 YGTNTTFQDWTKVTVYVNGVLVWGTEPSG 736

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; SEQ ID NO 5
; LENGTH: 101
; TYPE: PRT
; ORGANISM: Artificial Sequence

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```

/ GENERAL INFORMATION:
/ APPLICANT: DING, SHI-YOU
/ APPLICANT: ADNEY, WILLIAM S.
/ APPLICANT: VINZANT, TODD B.
/ APPLICANT: DECKER, STEPHEN R.
/ APPLICANT: HIMMEL, MICHAEL E.
/ TITLE OF INVENTION: THERMAL TOLERANT CELLULOSE FROM ACIDOTHERMUS
/ TITLE OF INVENTION: CELLULOLYTICUS
/ FILE REFERENCE: 40170.60S01
/ CURRENT APPLICATION NUMBER: US/09/917,383
/ CURRENT FILING DATE: 2001-07-28
/ NUMBER OF SEQ ID NOS: 14
/ SOFTWARE: PatentIn Ver. 2.1
/ SEQ ID NO 1
/ LENGTH: 1228
/ TYPE: PRT
/ ORGANISM: Artificial Sequence

```

;
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Segment of
; OTHER INFORMATION: Guxa
US-09-917-383-1

Query Match 90.6%; Score 491; DB 24; Length 1228;
Best Local Similarity 89.1%; Pred. No. 8.8e-44;
Matches 90; Conservative 3; Mismatches 8; Indels 0; Gaps 0;
Qy 1 GASCTATVYVNSDWGSGFTTATVTTGTGTRATSGTWTWSPAGNQTVTNYNTALTQSGK 60
Db 1128 GVACRATVYVNSDWGSGFTATVTTGTGTRATSGTWTWSPAGNQTVTNYNTALTQSGA 1187
Qy 61 SVTAKLSYNNVIOQGOSTTTFGNGSYSGTNTAPTLSCTAS 101
Db 1188 SVTATNLSYNNVIOQGOSTTTFGNGSYSGTNTAPTLSCTAS 1228

RESULT 6
US-09-917-384-1
; Sequence 1, Application US/09917384
; GENERAL INFORMATION:
; APPLICANT: DING, SHI-YOU
; APPLICANT: ADNEY, WILLIAM S.
; APPLICANT: VINZANT, TODD B.
; APPLICANT: DECKER, STEPHEN R.
; APPLICANT: HIMMEL, MICHAEL E.
; TITLE OF INVENTION: THERMAL TOLERANT CELLULOSE FROM ACIDOTHERMUS
; FILE REFERENCE: 40170.6US01
; CURRENT APPLICATION NUMBER: US/09/917,384
; CURRENT FILING DATE: 2001-07-28
; NUMBER OF SEQ ID NOS: 14
; SOFTWARE: Patent In Ver. 2.1
; SEQ ID NO 1
; LENGTH: 1228
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Segment of
; OTHER INFORMATION: Guxa
US-09-917-384-1

Query Match 90.6%; Score 491; DB 24; Length 1228;
Best Local Similarity 89.1%; Pred. No. 8.8e-44;
Matches 90; Conservative 3; Mismatches 8; Indels 0; Gaps 0;
Qy 1 GASCTATVYVNSDWGSGFTTATVTTGTGTRATSGTWTWSPAGNQTVTNYNTALTQSGK 60
Db 1128 GVACRATVYVNSDWGSGFTATVTTGTGTRATSGTWTWSPAGNQTVTNYNTALTQSGA 1187
Qy 61 SVTAKLSYNNVIOQGOSTTTFGNGSYSGTNTAPTLSCTAS 101
Db 1188 SVTATNLSYNNVIOQGOSTTTFGNGSYSGTNTAPTLSCTAS 1228

RESULT 7
US-09-917-383-8
; Sequence 8, Application US/09917383
; GENERAL INFORMATION:
; APPLICANT: DING, SHI-YOU
; APPLICANT: ADNEY, WILLIAM S.
; APPLICANT: VINZANT, TODD B.
; APPLICANT: DECKER, STEPHEN R.
; APPLICANT: HIMMEL, MICHAEL E.
; TITLE OF INVENTION: THERMAL TOLERANT CELLULOSE FROM ACIDOTHERMUS
; FILE REFERENCE: 40170.6US01
; CURRENT APPLICATION NUMBER: US/09/917,383
; CURRENT FILING DATE: 2001-07-28
; NUMBER OF SEQ ID NOS: 14
; SOFTWARE: Patent In Ver. 2.1
; SEQ ID NO 8

;
; LENGTH: 101
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Segment of
; OTHER INFORMATION: Guxa
US-09-917-383-8

Query Match 87.8%; Score 476; DB 24; Length 101;
Best Local Similarity 87.1%; Pred. No. 2e-43;
Matches 88; Conservative 3; Mismatches 10; Indels 0; Gaps 0;
Qy 1 GASCTATVYVNSDWGSGFTTATVTTGTGTRATSGTWTWSPAGNQTVTNYNTALTQSGK 60
Db 1 GVACRATVYVNSDWGSGFTATVTTGTGTRATSGTWTWSPAGNQTVTNYNTALTQSGA 60
Qy 61 SVTAKLSYNNVIOQGOSTTTFGNGSYSGTNTAPTLSCTAS 101
Db 61 SVTATNLSYNNVIOQGOSTTTFGNGSYSGTNTAPTLSCTAS 101

RESULT 8
US-09-917-384-8
; Sequence 8, Application US/09917384
; GENERAL INFORMATION:
; APPLICANT: DING, SHI-YOU
; APPLICANT: ADNEY, WILLIAM S.
; APPLICANT: VINZANT, TODD B.
; APPLICANT: DECKER, STEPHEN R.
; APPLICANT: HIMMEL, MICHAEL E.
; TITLE OF INVENTION: THERMAL TOLERANT CELLULOSE FROM ACIDOTHERMUS
; FILE REFERENCE: 40170.6US01
; CURRENT APPLICATION NUMBER: US/09/917,384
; CURRENT FILING DATE: 2001-07-28
; NUMBER OF SEQ ID NOS: 14
; SOFTWARE: Patent In Ver. 2.1
; SEQ ID NO 8
; LENGTH: 101
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Segment of
; OTHER INFORMATION: Guxa
US-09-917-384-8

Query Match 87.8%; Score 476; DB 24; Length 101;
Best Local Similarity 87.1%; Pred. No. 2e-43;
Matches 88; Conservative 3; Mismatches 10; Indels 0; Gaps 0;
Qy 1 GASCTATVYVNSDWGSGFTTATVTTGTGTRATSGTWTWSPAGNQTVTNYNTALTQSGK 60
Db 1 GVACRATVYVNSDWGSGFTATVTTGTGTRATSGTWTWSPAGNQTVTNYNTALTQSGA 60
Qy 61 SVTAKLSYNNVIOQGOSTTTFGNGSYSGTNTAPTLSCTAS 101
Db 61 SVTATNLSYNNVIOQGOSTTTFGNGSYSGTNTAPTLSCTAS 101

RESULT 9
US-09-917-383-6
; Sequence 6, Application US/09917383
; GENERAL INFORMATION:
; APPLICANT: DING, SHI-YOU
; APPLICANT: ADNEY, WILLIAM S.
; APPLICANT: VINZANT, TODD B.
; APPLICANT: DECKER, STEPHEN R.
; APPLICANT: HIMMEL, MICHAEL E.
; TITLE OF INVENTION: THERMAL TOLERANT CELLULOSE FROM ACIDOTHERMUS
; FILE REFERENCE: 40170.6US01
; CURRENT APPLICATION NUMBER: US/09/917,383
; CURRENT FILING DATE: 2001-07-28